

line. Support for these claims is found throughout the specification and specifically on pages 10-11 and 22. Amended Claims 59 and 60 are directed to methods of inducing insulin expression by expressing a protein with the sequence shown in SEQ ID NO: 1 in a mammal using *in vivo* and *ex vivo* methods respectively. Support for these claims is found throughout the specification and specifically on pages 5-6, 10-11 and 22.

Applicants also submit herewith a copy of a Declaration of Anne Reifel Miller, under 37 C.F.R. §1.132. (Exhibit A).

### 1. Claim Objections

The Examiner objected to Claim 34 as being in improper form because it was dependent on a canceled claim. The claim amendments presented above address this objection. Claim 34 has been canceled.

### 2. The Pending Claims are Fully Enabled for Purposes of 35 U.S.C. §112, Second Paragraph

The Examiner rejected Claims 20, 33 and 34 under 35 U.S.C. §112, second paragraph, as being indefinite. Claim 20 was rejected for use of the term "immunologically isolated." The Examiner stated that the term was "vague and indefinite." While Applicants disagree with the Examiner's assessment and point out that the term is discussed in the Specification (line 30, p. 10 through p. 11), Applicants have altered the claim term to "immunologically masked" in present Claims 35, 36, 49, 50 and 60 as suggested by the Examiner and believe this terminology satisfies the examiner's objection.

Claims 33 and 34 were rejected as being incomplete for missing process steps and as being unclear for not correlating the method to treatment of Type I and Type II diabetes.

Claims 33 and 34 were canceled and substituted with the present Claims 59 and 60 to which process steps were inserted and reference to treatment of Type I or Type II diabetes was removed.

3. The Pending Claims are Fully Enabled for Purposes of  
35 U.S.C. §112, First Paragraph

The Examiner rejected claims 19-34 under 35 U.S.C. §112, first paragraph, as not enabled by the specification. The basis for the Examiner's rejection appears to be that the specification provides insufficient guidance as to how to practice methods of treating Type I or Type II diabetes with the GLP-1-expressing cell lines of the invention. The Examiner also continues to assert that the specification does not provide enough guidance with respect to route of administration, dosage, targeting or expression level to enable specifically the treatment of diabetes. The Examiner argues that gene therapy is too unpredictable to warrant such claims given the amount of guidance in the specification.

Applicants have replaced the claims objected to with claims 59 and 60 to a method of inducing insulin expression in a mammal in need thereof. Claims 35-48 are directed to a stable cell line that expresses GLP-1, or an analog thereof, and Claims 49-58 are directed to a method of making said GLP-1-expressing cell line. Thus, this rejection is now moot.

Applicants believe the specification provides one of ordinary skill in the art with sufficient guidance to meet the enablement requirements of 35 USC §112 for the presently claimed invention. However, to further prosecution, a 37 C.F.R. §1.132 declaration by co-inventor Anne Reifel Miller, enclosed herein as Exhibit A, provides further evidence that a physiological effect results from the transplant of GLP-1-expressing cells of the invention into a mammal. The data

described in the declaration, generated following the teachings in the specification, demonstrate that an immunologically masked stable cell line expressing GLP-1 (or an analog thereof) induces insulin expression and decreases blood glucose levels in an individual in need thereof. A decrease in plasma glucose levels compared to control levels (Appendix A), and an increase in plasma insulin levels compared to control levels (Appendix B) was demonstrated in diabetic rats transplanted with cells from a stable mammalian cell line expressing a biologically active analog of GLP-1 and immunologically masked prior to transplantation.

It would not require undue experimentation for one of skill in the art to practice the presently claimed invention. The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation from the disclosure in the patent specification coupled with information known in the art at the time the patent applications was filed. *U.S. v. Teletronics, Inc.* 857 F.2d 778, (Fed. Cir. 1988). Enablement is not precluded even if some experimentation is necessary. *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367 (Fed. Cir. 1986). The need for some experimentation does not render the claimed invention unpatentable under 35 U.S.C. § 112. The dispositive issue is whether the disclosure would have enabled one of ordinary skill in the art to practice the invention without undue experimentation. In *re Strahilevitz*, 212 U.S.P.Q. 561, 563 (CCPA 1982). The focus is not on whether experimentation would be required, but whether such experimentation is undue. In analyzing this very issue, the Court of Appeals for the Federal Circuit ("CAFC") determined that experimentation, though laborious, is not undue experimentation when the specification provides a reasonable amount of guidance. In *re Wands* 858 F.2d 731 (Fed. Cir. 1988).

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Thus, based upon the information provided in the attached declaration, Applicants have demonstrated that a person of ordinary skill in the art would not have to undergo undue experimentation to practice the invention as presently claimed. For the Examiner to find otherwise would require the Examiner to come forward with evidence supporting a need for undue experimentation in order to enable the invention since the Applicant's specification and submitted declaration have demonstrated that the invention is enabled.

SUMMARY AND CONCLUSION

In view of the remarks and amendments enclosed and provided herein above, it is respectfully submitted that the Examiner's rejections have been overcome. Applicants request reconsideration and withdrawal of the rejections. If the Examiner feels that a telephone conversation with Applicants' Agent would be helpful in expediting the prosecution of this case, the Examiner is invited to call Applicants' Agent.

Respectfully submitted,



MaryAnn Wiskerchen  
Agent for Applicants  
Registration No. 45,511  
Phone: 317-655-9326

Eli Lilly and Company  
Patent Division/MC92H  
Lilly Corporate Center  
Indianapolis, Indiana 46285

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